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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/631,637	08/02/2000	Jean Gosselin	2097/49123	8660

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EXAMINER	
WINKLER, ULRIKE	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 07/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/631,637	Applicant(s) GOSSELIN ET AL.	
	Examiner Ulrike Winkler	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-56* is/are pending in the application.

4a) Of the above claim(s) *11-15 and 20-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-10 and 16-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 February 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The request filed on May 13, 2003 (Paper No. 18) for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/631637 is acceptable and a RCE has been established. Claims 1-3, 5-10 and 16-19 are pending and are currently under prosecution. An action on the RCE follows.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Request for interview

A request for an interview is a separate action and should not be part of the response (MPEP 713), when applicant is initiating a request for an interview, an "Applicant Initiated Interview Request" form (PTOL-413A) should be submitted to the examiner prior to the interview in order to permit the examiner to prepare in advance for the interview and to focus on the issues to be discussed. This form should identify the participants of the interview, the proposed date of the interview, whether the interview will be personal, telephonic, or video conference, and should include a brief description of the issues to be discussed.

Applicants have requested an interview in the RCE and response file in Paper No. 18, as a courtesy the Examiner made a telephone call to Applicants Representative J.D. Evans on July 15, 2003 in order to schedule an interview. No definite interview date has been scheduled.

Drawings

The Office acknowledges the submission of formal drawings on February 13, 2003 (Paper No. 14), the drawings have been accepted by the Draftsperson.

Claim Rejections - 35 USC § 112

The rejection of claims 1-3 6-10, 16-19 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention **is maintained** for reasons of record.

Applicants arguments presented in paper No. 19 have been considered but are not persuasive. Applicants arguments are: (1) that the commercial success is not a requirement for patentability; (2) that the Sandstrom et al. paper does not say suramin does not cause any immunological or clinical improvement; (3) applicant argue that they have done further experiments in SCID mice indicating that bpV prevents the loss of CD4+ cells; (4) the Barbeau et al. reference utilizes latently infected cells in which the virus is already integrated which is in contrast to applicants result that show bpV treatment prior to HIV infection would result in less cells being infected.

To address the arguments: (1) The Office agrees with the general principle set out in *In re Brana* 34 USPQ2d 1436. In *Brana* the question addressed was whether a compound had utility within the context of a 112 1st paragraph analysis. Obviously, if the invention has no utility then the specification cannot enable one to use it (see discussion). The courts indicated that there appeared confusion between the requirements under the law for obtaining a patent with the

requirements for obtaining government approval to market a particular drug for human consumption [citing *Scott v. Finney*, 34 F.3d 1058, 1063, 32 USPQ2d 1115, 1120 (Fed. Cir. 1994)]. The prior rejection of the instant invention was based on the necessity that a reasonable correlation must be made by applicant to show that compound would be effective in an *in vivo* setting. Applicants have submitted an exhibit in Paper No. 16 (note this was not in declaration form) indicating the use of bpV in an animal. The prior rejection of the instant invention was based on the dichotomy in the literature that indicates it is unpredictable to go from an *in vitro* [test tube] setting to a cure *in vivo* [animal] setting without some experimental evidence indicating that sufficient concentration can be achieved in the animal to result in the curative properties of the compound to be realized. This is a far cry from the highly stringent requirements that are set out by the FDA [fit for human consumption]. However, if a compound cannot be given in sufficiently high doses to be effective at inhibiting viral replication without causing detrimental effect in the subject it would seem obvious that the compound is not enabled. In *Brana* the question was whether animal testing provided sufficient *in vivo* data to be a reasonable predictive indicator of the effect of the compound in the human subject. The instant specification has not provided any in vivo data which could serve as an indicator of the effect in a patient.

(2) Applicant's arguments regarding the Sandstrom et al. paper are not persuasive; the reference was cited to point out that what is effective in the test tube is not necessarily reliably practicable in the body. Sandstrom et al. (page 376 column 2, paragraph 4) sets out that the adverse side effects where harmful in the patients tested, even though at high concentration they saw lowering of viral isolation. To reiterate the point of this reference is to indicate that

moving from an *in vitro* setting to an *in vivo* treatment is not predictable and must be tested. Because the levels of suramin would be toxic to the person suramin would not be a desirable drug candidate and thereby would not fulfill the role as an inhibitor of HIV. Therefore, the use of *in vitro* tests is not accepted as an indicator of *in vivo* activity of the compound, especially when the claimed invetion is drawn to a method of inhibiting viral infection in a patient.

(3) Applicant's point to a further example (Figure 9) provided in the their request for reconsideration (Paper No. 19) in which applicants have treated mice transplanted with CD4+ cells and infected with HIV and treatment with pbV. The figure indicates that CD4+ cell counts were made, implying that CD4+ cells are depleted by infection with HIV and therefore the increase of CD4 cells in the mice treated with pbV is an indication of viral inhibition. However, this experiment does not provide a measurement of the actual virus (such as p24 measurement or viral load measurement by PCR). An increased CD4+ count can be due to viral inhibition **or** it can be due to the effect of the compound resulting in the activation of T cells causing T cells replication which would explain the increase in CD4+ cells (see Barat et al. Journal of Biological Chemistry 2003). Without actually measuring viral indicators it is not possible to determine if the effect observed is due to viral inhibition by the compound.

(4) The arguments that Barbeau et al. uses latently infected cells vs. the newly infected cells used in the *in vitro* assay of the instant invention is not persuasive. In a "natural" HIV infection, after the initial viral infections which is followed by high levels of viral replication the virus becomes integrated into the genome and becomes latent. Therefore, assays that utilize latently infected cells may be more indicative of what goes on in an infected individual than in freshly infected cells. The prior art indicates that treating HIV infected cells with

peroxovanadium compounds causes activation of HIV transcription from the LTR (Barbeau et al., Journal of Biological Chemistry, 1997, see abstract and figure 1). The prior art also discloses an increase in the reverse transcriptase activity in the supernatant indicating that the treatment with peroxovanadium compounds results in an increase in particle release (see figure 8 and 9). Therefore, in light of the prior art it is not straight forward process to go from *in vitro* data to an *in vivo* treatment in combination with the information that the *in vitro* data presented in the present specification contradicts what is known in the prior art, indicating that the instantly claimed treatment highly unpredictable. Thus, the lack of working examples regarding treatment of any retroviral infection including HIV in a patient, the lack of guidance in the specification, and the unpredictability regarding extrapolating *in vitro* data to an *in vivo* treatment method greatly reduces the probability that one of skill in the art would successfully obtain the claimed invention without undue experimentation.

The rejection **is maintained**.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ULRIKE WINKLER, PHD.
PATENT EXAMINER

7/18/05